PATENT COOPERATION TREATY

# PCT



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference<br>4-32557A | **FOR FURTHER ACTION** | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No.<br>PCT/EP 03/07198 | International filing date *(day/month/year)*<br>04.07.2003 | Priority date *(day/month/year)*<br>05.07.2002 |
| International Patent Classification (IPC) or both national classification and IPC<br>C07D401/14 | | |
| Applicant<br>NOVARTIS AG et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 19.01.2004 | 17.08.2004 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized Officer<br>Timmermans, M<br>Telephone No. +49 89 2399-8940 |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/07198

## I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

**Description, Pages**

| | |
|---|---|
| 1-70 | as originally filed |

**Claims, Numbers**

| | |
|---|---|
| 1-7, 11 (part), 12-14 | as originally filed |
| 8-10, 11 (part) | received on 03.08.2004 with letter of 03.08.2004 |

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 13

   because:

   ☒ the said international application, or the said claims Nos. 13 relate to the following subject matter which does not require an international preliminary examination (specify):

   **see separate sheet**

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-14 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-14 |
| Industrial applicability (IA) | Yes: | Claims | 1-12,14 |
| | No: | Claims | |

2. Citations and explanations

   **see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. Claim 13. relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The following documents are relevant:
   - D1: ZIMMERMANN J ET AL: 'Potent and selective inhibitors of the Abl-kinase: phenylamino-pyrimidine (PAP) derivatives' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 7, no. 2, 21 January 1997 (1997-01-21), pages 187-192, XP004135990 ISSN: 0960-894X
   - D2: ZIMMERMANN J ET AL: 'Phenylamino-pyrimidine (PAP) - derivatives: a new class of potent and highly selective PDGF-receptor autophosphorylation inhibitors' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 6, no. 11, 4 June 1996 (1996-06-04), pages 1221-1226, XP004134858 ISSN: 0960-894X
   - D3: EP-A-0 588 762 (CIBA GEIGY AG) 23 March 1994 (1994-03-23)
   - D4: PAUL R ET AL: 'Preparation of substituted N-phenyl-4-aryl-2-pyrimidinamines as mediator release inhibitors' JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 36, no. 19, 17 September 1993 (1993-09-17), pages 2716-2725, XP002134022 ISSN: 0022-2623
   - D5: WO 95 09853 A (CIBA GEIGY AG ;ZIMMERMANN JUERG (CH)) 13 April 1995 (1995-04-13)

2. The novelty of the subject-matter of the present application is acknowledged. (Art. 33(2) PCT).

2.1 The compound originally claimed in claim 10 which lacked novelty has been removed form the current set of claims.

2.2 The compounds which are the object of the present application differ from the other compounds disclosed in D1 by the amide function attached to the phenyl ring. Nevertheless, document D1 discloses several phenylaminopyrimidine derivatives which are structurally close to the compounds of the present application: see D1, Table 1, Column A, examples No 17 and 24 or compound 1, page 189. All those compounds are usefull against leukemia.
The same consideration applies to document D2: see D2, page 1223, Examples No 3 and 11.

2.3 The compounds of the present application differ from the ones disclosed in D3 by the nature of the groups $R^1$ - $R^2$, which are never alkylamino like in D3, from the ones disclosed in D4 by the nature of the phenyl subsitutents and from the ones disclosed in D5 by the substitution pattern of the pyridinyl ring.

3. The set of claims of the present application is considered as lacking an inventive step (Art. 33(3) PCT).

3.1 Documents D1 and D2, which are considered to represent the most relevant state of the art, disclose phenylaminopyrimidine derivatives usefull against leukemia from which the compounds of the present application differ only in the attachment of the amide function.

3.2 The problem to be solved by the present invention may therefore be regarded as the further provision of phenylaminopyrimidine derivatives usefull against leukemia.

3.3 Starting from the teaching of D1 or D2, it is considered that the compounds of the present application are the results of slight structure modifications (i.e. the inversion of an amide function), which come within the scope of the customary practice followed by the man skilled in the art of analog synthesis.

3.4 The subject-matter of the present application could only be regarded as inventive, if the compounds objects of the present application would present unexpected effects or properties in relation to those described in the state of the art.
As far as no unexpected properties compared with the structurally closest compounds of D1 and D2 (e.g. D1, compound 1 and D2, compounds 4 and 9) were shown, the compounds of the present application do not meet the requirements of Article 33(3) EPC.

4. The industrial applicability of claims 1-12 and 14 is acknowledged (Art. 33(4) PCT).

4.1 For the assessment of the present claim 13 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.